



24 **ABSTRACT**

25 **Objective:** To evaluate if pharmacy students' participation in personal pharmacogenetic  
26 (Pgx) testing enhances their knowledge and attitude towards precision medicine (PM).

27 **Methods:** First-year pharmacy students were offered personalized pharmacogenetic  
28 testing as a supplement to a required curricular pharmacogenomics course. Ninety-  
29 eight of 122 (80%) students completed pre- and post-course surveys assessing  
30 knowledge and attitudes regarding PM; 73 students also volunteered for personal  
31 pharmacogenetic testing of the following drug metabolizing enzymes (*CYP2C19*,  
32 *CYP2D6*, *UGT1A1*) and pharmacodynamics-relevant proteins (interleukin (IL)-28B &  
33 human lymphocyte antigen HLAB\*5701).

34 **Results:** Using a linear mixed effects model, we observed statistically significant  
35 improvements in 100% of knowledge and 70% of attitude-related questions for students  
36 who decided to undergo personal pharmacogenetic testing.

37 **Conclusion:** Personal pharmacogenetic testing significantly enhances knowledge of  
38 and attitude related to precision medicine among PharmD trainees. This study  
39 demonstrates the feasibility and importance of educating future pharmacists by  
40 incorporating pharmacogenetic testing into professional school curricula.

41  
42 **Keywords:** pharmacogenomics, genotyping, pharmacy curriculum, pharmacogenetics,  
43 personal pharmacogenetics

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## 47 INTRODUCTION

48 The Human Genome Project laid the groundwork in 2003 for an innovative  
49 approach to medicine that we today call Precision Medicine.<sup>1</sup> This new era of medicine  
50 is centered around combating human diseases through prevention and treatment,  
51 based on lifestyle, environment and genetics, serving as the basis for President  
52 Obama's Precision Medicine Initiative in 2015.<sup>2</sup> The impact of precision medicine in the  
53 clinical setting today can be observed through the lens of pharmacogenetics. This term  
54 was used as early as 1959, when inter-individual drug response was attributed to  
55 genetic variation<sup>3</sup> and is particularly apparent today in the setting of clinical oncology.<sup>4-6</sup>

56 In order for this new era of "precision medicine" to become accepted into clinical  
57 practice, we must start by educating our future healthcare providers and clinicians. In  
58 our current landscape there have been a number of studies<sup>3,7-14</sup> with promising  
59 outcomes regarding the impact of including some form of pharmacogenomics-related  
60 education in graduate school curricula. Unfortunately, the uptake into U.S. pharmacy  
61 programs still remains minimal. This is evident by a report in 2010 that surveyed the  
62 number of hours U.S. pharmacy schools were dedicating to pharmacogenomics-related  
63 education. Only 14.5% of schools surveyed spent between 31-60 hours on  
64 pharmacogenomics-related topics, and a majority of respondents described the present  
65 state of pharmacogenomics instruction at most schools of pharmacy as "poor."<sup>15</sup>

66 Efforts at using genotyping as a teaching supplement have been described,<sup>7,8,11-</sup>  
67 <sup>14</sup> catalyzing the movement towards the adoption of pharmacogenomics into graduate  
68 school curricula. Our study aims to add to this body of knowledge by providing personal  
69 pharmacogenetic testing to first year pharmacy students as an adjunct to a curricular

70 pharmacogenomics course to gauge the impact on knowledge and attitude. This project  
71 is innovative as it emphasizes several key themes: 1. students have the autonomy to  
72 choose the most relevant gene to have genotyped based on their race or personal  
73 desire; 2. the project is the result of a student-led initiative; 3. the project focuses solely  
74 on pharmacogenetic variants, avoiding potential controversy that some direct-to-  
75 consumer tests faced when providing disease risk assessments; 4. the implementation  
76 is feasible; and 5. the findings are very robust.

77

## 78 **METHODS**

### 79 **Background**

80 Prior to our current assessment, a smaller pilot study was conducted among first-  
81 year PharmD students at UCSF. Biopharmaceutical Sciences (BPS) 115 (“Genetics and  
82 Pharmacogenetics”) is a required (curricular) pharmacogenomics course in the School  
83 of Pharmacy. Objectives for BPS 115 are broadly based and derived from components  
84 of genetic competencies put forth by the Accreditation Council for Pharmacy  
85 Education.<sup>16</sup> Twenty-two students enrolled in the spring 2013 BPS 115 course  
86 volunteered to have their DNA isolated from blood samples and genotyped for variants  
87 in *CYP2C19*, a common drug metabolizing enzyme that is important in metabolizing  
88 several therapeutic agents including clopidogrel, a widely used anti-platelet agent. The  
89 course directors chose to genotype *CYP2C19* because variants in this gene are known  
90 to vary by race, and aside from the ability to metabolize certain drugs, the variants are  
91 not known to convey disease risk. This circumvents potential ethical issues that may  
92 arise when disclosing disease risk. Some universities offering genomic testing for

93 genetic diseases were criticized for failing to provide genetic counseling or conducting  
94 testing in a non-CLIA-certified laboratory.<sup>17</sup>

95         The BPS 115 course directors held a lecture session to disclose the results of the  
96 students' genotypes. During this session, course directors reviewed the clinical  
97 implication in terms of drug metabolism of different variants of *CYP2C19*. Following the  
98 session, students organized a focus group to ask faculty more questions and create a  
99 space for students to continue sharing their learnings and genotypic information with  
100 other interested classmates. Students provided a substantial amount of feedback, which  
101 was recorded and used to develop a formal study protocol. They unanimously  
102 expressed the value of the testing and use of the results as teaching material for the  
103 course. Students discussed why it was compelling and crucial to their future as  
104 pharmacists and the future of their profession. A sample of representative, unsolicited  
105 student comments regarding their experience include:

- 106
- 107         • *“I see personal pharmacogenetic testing in the future of pharmacy. It can be time saving.*  
108             *It is going to be dependent on factors like whether MDs are willing to order genotyping*  
109             *tests instead of starting empirical therapy and dosing, and if we will begin educating our*  
110             *future clinicians. Implementation will require a new generation of MDs/pharmacists to*  
111             *lead this movement.”*
  
  - 112
  - 113         • *“Information outside of academia regarding pharmacogenomics is limited. Many people*  
114             *in the public are not aware that testing is even available. As leaders/graduates from this*  
115             *university, we have to communicate our knowledge to outside communities and the rest*  
116             *of the world. Having a diverse group of people communicating this information will*

117 *spread the word about needing research in more ethnically diverse populations.*

118 *Pharmacists will be the most easily accessible group of healthcare practitioners, so*

119 *questions about testing will go to us before many in the hospital.”*

120

121 • *“I genuinely enjoyed the class, and I learned a lot. This information inspires me to want*

122 *to look further into why certain populations are fast metabolizers, or slow metabolizer or*

123 *do not respond well to certain medications. I would like to personally be involved in*

124 *pharmacogenomics in the future during my career.”*

125

## 126 **Survey Design**

127 Based on the pilot study’s overwhelmingly positive feedback, personal

128 pharmacogenetic testing was incorporated into BPS 115 the following year on a

129 volunteer basis. BPS 115 is part of the core curriculum at the UCSF School of

130 Pharmacy. However, voluntary personal pharmacogenetic testing was temporarily

131 added into the course during the spring 2014 term. One month before the start of the

132 term, an online Likert survey was administered to 122 first-year UCSF School of

133 Pharmacy (SOP) students enrolled in BPS 115.

134 Survey development was informed by the focus group conducted among the 22

135 students from the spring 2013 BPS 115 class. We used students’ responses to identify

136 themes to guide development of questions designed to assess students’ attitudes and

137 knowledge towards precision medicine. A draft of the survey was then piloted among a

138 sample of second-year pharmacy students; these results were used to fine-tune the

139 survey. First-year students were excluded from the design process to avoid influencing

140 them during the actual assessment. We chose a Likert-based response format because

141 its common use lends itself to easy understanding by respondents, and their answers  
142 can easily be quantified and used in statistical tests. Survey questions are summarized  
143 in Supplementary Table 1.

144 The survey was re-administered to the same first-year students following  
145 completion of the 10-week course. In addition to knowledge- and attitude-assessment  
146 questions in the post-course survey, we also asked separate reflection questions,  
147 allowing us to assess students' opinions about participating in pharmacogenetic testing.  
148 The knowledge, attitude, and reflection questions are listed in Supplemental Table 1.

149 Expected outcomes included the following three objectives: (1) increasing  
150 understanding of pharmacogenetic concepts in relation to clinical applications, (2)  
151 changing attitude toward precision medicine and clinical integration of  
152 pharmacogenetics, and (3) enhancing classroom learning of the subject matter  
153 (pharmacogenomics).

154

## 155 **Survey Assessment**

156 The voluntary pre- and post-course survey and pharmacogenetic testing were  
157 approved by the UCSF Committee on Human Research. Written consent and email  
158 addresses were collected from all students who were interested in participating in the  
159 survey. Email addresses were entered into UCSF's Research Electronic Data Capture  
160 (REDCap) system, a secure online utility for conducting surveys. Once a student logged  
161 on to REDCap to take their survey, REDCap would automatically generate and assign  
162 an anonymized, unique identifier linked to login information. The same identifier was

163 associated with all surveys that the subject completed ensuring no surveys were lost  
164 due to individuals forgetting their own self-assigned survey numbers.

165 While the survey asked for basic personal information, REDCap only exported  
166 the assigned identifier with the survey data. To ensure that participation was voluntary,  
167 the names and email addresses associated with the survey results remained restricted  
168 from both primary researchers and course faculty members. Only the primary  
169 researchers were authorized to access the de-identified REDCap data (the course  
170 directors were not involved in the survey-based assessment).

171

## 172 **Pharmacogenetic Testing**

173 During the course, students had the opportunity to volunteer to have their own  
174 DNA genotyped for several drug metabolizing enzymes as a “hands-on” personal  
175 pharmacogenetic learning experience as a supplement to the curricular course (BPS  
176 115). Several days were coordinated to collect de-identified saliva samples from  
177 students. The samples were analyzed in a UCSF-affiliated CLIA-certified laboratory at  
178 San Francisco General Hospital at the rate of \$50 per genotype. For the 73 students  
179 who participated in genotyping, the total cost was \$3,650, which excludes the time the  
180 laboratory donated to analyze the samples. Genotyping costs were generously covered  
181 by the UCSF School of Pharmacy. Since genotyping was not performed through a  
182 commercial supplier, the results were ready much sooner than the 3-6 week turnaround  
183 time often seen with direct to consumer genetic testing companies. The total time for  
184 participant consent and recruitment, DNA collection, genotyping, and presentation of the  
185 data was approximately 150 person-hours. Students were given the option to have

186 genotyped either a gene for a drug metabolizing enzyme (*CYP2C19*, *CYP2D6*, or  
187 *UGT1A1*) or a pharmacodynamics-relevant protein (*IL28B* or *HLAB\*5701*). Each of the  
188 genes coding these enzymes/proteins has its own unique clinical implication and  
189 varying allele frequency (and therefore varying activity) among ethnic groups (Table 1).

190

## 191 **Unveiling of Pharmacogenetic Results**

192       Once genotyping was completed, students were given their personal  
193 pharmacogenetic information during a regularly scheduled class period for BPS 115; the  
194 class session was divided into two sessions. During the first session, a  
195 pharmacogeneticist was invited to review and discuss each of the genes under  
196 evaluation, their variants, clinical significance, and how this information might be  
197 incorporated into clinical practice illustrated through clinical cases. At the end of this  
198 discussion, the pharmacogeneticist displayed each of the possible genes via  
199 PowerPoint slides and revealed each of the possible variants. Next to each variant was  
200 a list of anonymized identifiers so that students were able to privately determine their  
201 individual genotype status. The first part of the session was didactic, while the teaching  
202 methodology used in the second half of the session emphasized an *active learning*  
203 *classroom model* in which students were given 15 minutes to discuss the cases  
204 presented by the pharmacogeneticist among each other, and then initiate an open  
205 discussion about how different variants may affect pharmacologic or medical  
206 management. During the open discussion, students engaged in an active question and  
207 answer session with each other and the pharmacogeneticist; discussions were centered  
208 around the presented pharmacogenetic information and clinical cases. Students based

209 many of their questions and comments on their personal pharmacogenomic data as  
210 they discussed potential pharmacologic alternatives and pharmacologic interventions  
211 (e.g., dose reductions, discontinuation of meds, drug-drug interactions) to account for  
212 potential variants. Additionally, students expressed interest in strategies for pharmacists  
213 to play a more active role in the future of this specialty. This session did not require  
214 specific preparatory work besides attending the course lectures and completing  
215 assigned readings<sup>18–20</sup> throughout the course (pertaining to the course and basic  
216 concepts of pharmacogenetics).

217

## 218 **Statistical Analysis**

219 We defined our outcome as change in knowledge or attitude regarding precision  
220 medicine. Specifically, we assigned integer values to the 5-point Likert scale (i.e., 1 =  
221 strongly disagree, 2 = disagree, 3 = neutral, 4 = agree and 5 = strongly agree) and then  
222 examined the change in Likert scores for each knowledge and attitude question by  
223 calculating the difference between pre- and post-survey responses. For example, a pre-  
224 survey response of 3 (neutral) followed by a post-survey response of 4 (agree) to the  
225 same question would be a gain of 1 Likert point. This difference served as our  
226 dependent variable. Our analysis was stratified into two groups: (1) students who  
227 participated in the personal genotyping and the survey (the genotyped group), and (2)  
228 those who participated in the survey, but not in personal genotyping (the non-genotyped  
229 group). The effect of the pharmacogenetic testing on knowledge and attitude was  
230 estimated using linear mixed effects analysis. We used a linear mixed effect approach  
231 to account for unmeasured time-dependent variables. For example, the passage of time

232 between the pre- and post-course surveys could have influenced knowledge and  
233 attitude independently of the curriculum and our study. In addition, this approach also  
234 allows us to estimate the effect of the curriculum after accounting for sex and race,  
235 unlike a bivariate statistic (e.g., T-test). Variables for sex and race were included as  
236 fixed effects, with a random intercept for student. Estimates whose confidence intervals  
237 excluded the null value were considered statistically significant at an alpha level of 0.05.  
238 Survey results were analyzed using the lme4 package<sup>21</sup> in the R statistical programming  
239 language (R Core Team, 2015).<sup>22</sup>

240

## 241 **RESULTS**

242 In total, 98 (80%) of the 122 students enrolled in the spring 2014 BPS 115 course  
243 voluntarily completed the pre- and post-course surveys. Of these 98, 73 (74.5%)  
244 students also took part in genotyping, leaving 25 students (25.5%) to comprise the  
245 surveyed but not genotyped group. Selected demographic characteristics of the  
246 students are summarized in Table 2. The genotyped group had significantly more  
247 females than the non-genotyped group but the two groups did not significantly differ by  
248 race/ethnicity. Attitudinal and knowledge assessment was performed via an electronic  
249 online survey using a Likert scale response format. Baseline scores in knowledge and  
250 attitude were similar for both groups. The mean baseline Likert score for knowledge  
251 questions was (3.03) in the genotyped group and (3.14) in the non-genotyped group.  
252 For the attitude questions, the mean baseline score was (3.85) in the genotyped group  
253 and (3.83) in the non-genotyped group.

254           The results for change in knowledge and attitude are stratified by genotyping  
255 status and summarized in Figures 1 and 2, respectively. We limited our analysis to  
256 results with a minimum effect size of 0.25 Likert points (i.e., a difference in means  
257 between pre- and post-survey results of 0.25 Likert points). This was set as an arbitrary  
258 cut-off, and we concluded that any positive change in the Likert scale that is at least  
259 0.25 points and effect estimates whose confidence intervals excluded the null value  
260 (i.e., 0) were determined to be statistically significant.

261           One-hundred percent of responses to the knowledge questions showed  
262 statistically significant improvement between pre- and post-survey assessments,  
263 regardless of whether students participated in genotyping. The smallest increase in  
264 estimates was 0.64, which is more than double our minimum effect size cut-off of 0.25.  
265 The mean change in knowledge across all knowledge questions was not significantly  
266 different between the genotyped (0.99) and non-genotyped (1.05) groups ( $p = 0.68$ ).  
267 Seventy percent of the attitude questions in students who underwent genotyping  
268 showed a statistically significant improvement in the pre- and post-Likert scores. In the  
269 non-genotyped group, however, only forty percent of the attitudinal questions showed  
270 significant improvement. While the mean change in attitude was slightly higher among  
271 those who did not participate in genotyping (0.36) versus those who did (0.30), the  
272 difference was not statistically significant ( $p = 0.31$ ). The correlation between pre- and  
273 post-survey responses was fairly consistent for knowledge (Pearson's  $r = 0.63$ ) and  
274 attitude ( $r = 0.62$ ) questions.

275           In the genotyped group, the knowledge assessment question with the largest  
276 increase (1.32 Likert points, 95% confidence interval [CI]: 1.10-1.53) asked students to

277 identify with the following statement: “I am aware of the types of knowledge and  
278 resources needed to interpret a pharmacogenetic test” (Knowledge Question 4,  
279 Supplementary Table 1 and re-titled “Interpreting Pgx tests in Figure 1). Among the non-  
280 genotyped group, the knowledge assessment question with the largest increase (1.32,  
281 95% CI: 1.01-1.63) asked students whether they “...understand how to evaluate the  
282 clinical validity and utility of a pharmacogenetic test” (Knowledge Question 5,  
283 Supplementary Table 1, and shown in Figure 1). The attitude assessment question with  
284 the largest increase was the same for genotyped (0.52, 95%CI: 0.34-0.70) and non-  
285 genotyped (0.52, 95%CI: 0.20-0.84) students. This question asked students whether  
286 “Pharmacogenetic testing, when applicable, should be integrated into patient care”  
287 (Attitude Question 6, Supplementary Table 1). The 95% confidence interval for this  
288 question, however, was much narrower and more robust for the genotyped group as  
289 illustrated in Figure 2.

290 We also asked students to reflect on their experiences being a part of this pilot  
291 project. We categorized these reflections as “genotyped group” versus “non-genotyped  
292 group.” Students were more likely to have favorable impressions of precision medicine if  
293 they were in the genotyped group versus those in the non-genotyped group. Among the  
294 73 students who were genotyped, 89% said that they were glad to have participated,  
295 and 85% stated that they had a better understanding of the principles of  
296 pharmacogenetics. Furthermore, 77% of the genotyped group said they felt more  
297 engaged during BPS 115, and 83.5% agreed that their participation in genotyping  
298 reinforced the concepts taught in the course (Table 3).

299 For the non-genotyped group, 60% regretted their decision and the same 60%  
300 stated that they would choose to undergo pharmacogenetic testing if it was offered to  
301 them again. Sixty-eight percent of students in the non-genotyped group stated that  
302 concepts taught in the course were reinforced after seeing their classmates receive their  
303 genetic results. Lastly, 68% of students in the non-genotyped group said they would be  
304 interested in participating in more comprehensive genetic testing to learn about other  
305 traits (Table 3).

306

## 307 **DISCUSSION**

308 We found that incorporating genetic testing as an adjunct to School of Pharmacy  
309 PharmD curriculum significantly enhanced students' knowledge and attitudes of  
310 precision medicine. In both the genotyped and non-genotyped groups, there was an  
311 increase in all of the knowledge assessment questions before and after the study. This  
312 finding provides strong support that an interactive hands-on approach to educating  
313 future pharmacists about pharmacogenetics is a fundamental curricular change that  
314 would benefit professional doctorate programs. As pharmacogenomics becomes  
315 increasingly fundamental for pharmacists in our health system, knowledge and  
316 acceptance of this new era of precision medicine is required for pharmacists to begin  
317 designing and developing personalized pharmacotherapy.

318 Efforts at pharmacogenetics education have been made in the past. A  
319 genotyping exercise was piloted in 2009 by Knoell et al. at The Ohio State University<sup>13</sup>  
320 where authors collected DNA samples from 10 PharmD student volunteers to genotype  
321 the Angiotensin Converting Enzyme (ACE) gene. Results were presented and

322 discussed in a classroom setting in the context of a patient-counseling workshop. Their  
323 Likert-based survey results demonstrated that 85% of students either agreed or strongly  
324 agreed that “the genotyping exercise was beneficial in terms of helping them better  
325 connect to course content.”<sup>13</sup> Nearly one-third of those students also stated that they  
326 would have liked to see more relevant genes being tested. This observation  
327 underscores why our study emphasized students’ autonomy regarding which gene they  
328 chose to be genotyped for.

329         A 2009 study conducted at Temple University School of Pharmacy took a  
330 laboratory based approach to increase pharmacy student understanding of  
331 pharmacogenomics. The study involved 70 second-year PharmD students and an  
332 analysis of single nucleotide polymorphisms of the *NAT2* gene based on DNA extracted  
333 from their saliva.<sup>8</sup> The study concluded that a laboratory session in pharmacogenomics  
334 was beneficial in helping students understand the relevance of pharmacogenomic  
335 analysis in designing/creating a patient medication regimen.<sup>8</sup> Similarly, a pilot study by  
336 Kisor et al. explored a curricular based laboratory course in which PharmD students  
337 used their own DNA (buccal swab) to genotype cytochrome P450 2C19 using PCR and  
338 gel electrophoresis. These results were successfully used to arrive at a “clinical  
339 decision” based on a dosing algorithm relative to the use of clopidogrel.<sup>11</sup>

340         Another innovative study in 2013 by Salari and colleagues conducted at Stanford  
341 University’s School of Medicine included personalized pharmacogenetic testing as an  
342 interactive supplement to an elective course for medical students. That study found a  
343 statistically significant impact on enhancing medical student knowledge and attitudes  
344 towards personal genome testing and precision medicine.<sup>7</sup> In 2014 at Ohio Northern

345 University, Bova et al. implemented a web-blog based introduction to pharmacogenetics  
346 and precision medicine as an elective course in the PharmD curriculum. Although  
347 students did not undergo personal pharmacogenetic testing, results of a pre- and post-  
348 course survey demonstrated a statistically significant improvement in a majority of  
349 questions relating to students' knowledge of pharmacogenetics and precision  
350 medicine.<sup>12</sup>

351 Most recently in 2016, Adams et al. published promising results from the  
352 University of Pittsburgh demonstrating significant improvements in PharmD students'  
353 knowledge and attitude after participating in personal pharmacogenetic testing.  
354 Students were genotyped using commercial genetic testing supplied by 23andMe,<sup>14</sup>  
355 which raised some questions about the potential to discover undesired information  
356 about genetic disease risk. Efforts were made to mitigate this risk by focusing on  
357 pharmacogenetics genes, but the raw data provided by 23andMe to each consumer  
358 includes data about other non-pharmacogenetic genes. The ethics of uncovering  
359 genetic disease risk is a serious consideration when choosing how to provide personal  
360 pharmacogenetic testing to students. In our study, we desired to eliminate the chance of  
361 conveying any sort of disease risk by focusing on a selected number of genes that were  
362 solely pharmacogenetically relevant.

363 The results presented in our innovative curricular approach to increasing  
364 knowledge and improving attitudes towards pharmacogenetic testing and precision  
365 medicine are encouraging. The overwhelming majority (80%) of students completed  
366 pre- and post-course surveys, and 75% of them took part in personal pharmacogenetic  
367 testing, which is significant considering the novelty of this idea to students and our

368 curriculum. Based on our experience, implementing personal pharmacogenetic testing  
369 across all US pharmacy school curricula would not be extremely arduous. Student  
370 participation was very high in the absence of incentives; the time and effort dedicated  
371 toward collection and processing of DNA was fairly minimal; performing genotyping in-  
372 house was orders of magnitude less expensive than commercially available tests; and  
373 the discussion of genotyping results was limited to only one class session. Instructors  
374 could limit their selection of genetic tests to inexpensive ones to optimize widespread  
375 dissemination of an educational session of this type. Educating our future providers and  
376 providing them with tools to adequately adapt and provide for their patients in an ever-  
377 changing healthcare landscape is a worthwhile investment if we wish to adequately  
378 incorporate pharmacogenetics into medical practice.

379         One of our most noteworthy findings was in regard to Knowledge Question #4  
380 (Supplementary Table 1): “I am aware of the types of knowledge and resources needed  
381 to interpret a pharmacogenetic test.” The effect size was fairly large among genotyped  
382 students, (1.32, 95%CI: 1.10-1.53), demonstrating that students felt confident utilizing  
383 their resources to interpret a pharmacogenetic test. This observation suggests that a  
384 curriculum designed to include similar personal pharmacogenetic testing will prepare  
385 students to keep up with the precision medicine revolution and ensure that patients are  
386 being treated by a confident and knowledgeable health care professional.

387         Sixty-eight percent of non-genotyped students reported that their classmates’  
388 participation in genotyping positively impacted their learning in the course, as described  
389 in the evaluation and assessment section above. This underscores the impact that the  
390 shared experience of personal pharmacogenetic testing had and the potential it has in

391 educating our providers who do not wish to undergo pharmacogenetic testing  
392 themselves. Although the impact was less for the non-genotyped group, specifically in  
393 terms of attitudinal assessment, this information is still important when considering  
394 curricular redesign as it allows various interventions or combinations of them to be  
395 utilized to achieve maximal learning outcomes. Sixty percent of the non-genotyped  
396 students also mentioned that they regretted their decision not to volunteer for personal  
397 pharmacogenetic genotyping, which illustrates how the idea of Pgx is still new and will  
398 require some more research and time to become commonplace. It is evident that the  
399 experience is a shared and interactive one that not only stems from one's own personal  
400 pharmacogenetic information, but also from that of his/her peers.

401         Barriers to the acceptance of Pgx are multi-faceted and one method for  
402 increasing acceptance is to break inter-professional barriers. Calinski and Kisor provide  
403 an example of lessons learned when physician assistant students and pharmacy  
404 students discuss cases related to the pharmacogenomics of Plavix (clopidogrel).<sup>10</sup> It is  
405 important that health care professionals understand not only their roles and impact in  
406 regards to precision medicine and Pgx but also the impact and role of their health care  
407 professional counterparts.

408         Potential biases should be considered when reviewing the results of our study.  
409 Knowledge and attitude were measured by self-assessment. This method is not as  
410 robust as objective data, but given the ubiquitous use of surveys as well as the logistical  
411 restraints of adding personal pharmacogenetic testing into an already established  
412 curricular course, self-assessments were a viable option. Some unmeasured  
413 characteristics of genotyped students (e.g., attitudes toward providing biological

414 samples) may have differed from non-genotyped students such that comparison of pre-  
415 /post- results between these two groups would not be valid (i.e., selection bias).

416 However, we found no significant difference in baseline knowledge or attitude between  
417 the two groups. Nonetheless, it is possible that participants who elected to be

418 genotyped would be more receptive to pharmacogenetics and thus that their attitudes  
419 would improve by a larger share than those who elected not to be genotyped. Although

420 we found that 40% of the attitude questions showed a significant improvement among  
421 students who elected not to be genotyped, compared to 70% for those students in the

422 genotyped group, the results for the non-genotyped group may have been

423 underpowered given the smaller number of students who chose to be genotyped (25

424 versus 73). It is also possible that students who volunteer for genotyping may naturally

425 be more inclined to have a positive attitude towards the topic at hand versus those who  
426 chose not to be genotyped. Given that the effect estimates for all knowledge and

427 attitude assessment questions were positive, regardless of genotyping status, we feel

428 that the influence of this type of selection bias is minimal. Our analyses were conducted

429 under the assumption that the intervals between Likert values are equal. We felt it

430 reasonable, for example, to assume that “Agree” is halfway between “Neutral” and

431 “Strongly agree;” this is a common assumption practiced in analysis of survey results.<sup>23</sup>

432 It is likely that even students who elected not to be genotyped benefitted from the

433 *active classroom model* in which students were given 15 minutes to share and discuss

434 results with all students, followed by an open discussion revolving around the clinical

435 cases and information presented by the pharmacogeneticist. The gain in knowledge and

436 attitude for both the genotyped and non-genotyped group is interesting and questions

437 whether our results are attributable to personal pharmacogenetic testing versus  
438 traditional didactic coursework. The difference in improvement between groups is  
439 greater for the knowledge-related items than for attitude, consistent with the belief that  
440 knowledge affects attitude, which in turn affects behavior.<sup>24,25</sup> The genotyped group had  
441 tighter confidence intervals and more robust data as we would have expected based on  
442 sample size. However, that both groups improved in knowledge and attitude is  
443 encouraging, suggesting that once participation in genetic testing surpasses some  
444 threshold, non-genotyped students may learn vicariously through experiences and  
445 learning environment created by genotyped students. In essence, the rising tide of  
446 pharmacogenetic education lifted all boats.

447         Isolating the impact of genetic testing without overly-disrupting the course  
448 structure posed logistical challenges. As with intervention trials, preventing crossover  
449 (e.g., non-compliance or contamination) between treatment groups would have been  
450 difficult. Ideally, students would have been randomized into testing and non-testing  
451 groups prior to the start of the course. The course material for these two groups would  
452 then have been presented separately, in effect creating two versions of BPS 115 (one  
453 for those randomized to genetic testing and another for those not receiving genetic  
454 testing). This approach imposed too many logistical restrictions.

455         In order to overcome these limitations, a future cluster-based randomized study  
456 with several pharmacy school curricula could be implemented. Since self-efficacy—  
457 which was not measured in this study—is useful for predicting future behavior, we plan  
458 to contact these students for a long-term follow-up to assess the lasting effects that  
459 personal pharmacogenetic testing has had on their personal and professional lives.

460 Furthermore, we hope that this study serves as a means to further accelerate the  
461 dissemination of personal pharmacogenetic testing into U.S. pharmacy school curricula.

462

## 463 **SUMMARY**

464 Pharmacy students in their first year of the PharmD curriculum showed  
465 significant enhancements in their knowledge and attitudes towards precision medicine  
466 after participating in personalized pharmacogenetic testing. Even students who were  
467 enrolled in the course but did not partake in personalized pharmacogenetic testing had  
468 an enhancement in knowledge and attitude about precision medicine, likely as a result  
469 of engagement with their classmates and faculty regarding the results. This dynamic  
470 allows more room for pharmacy schools to personalize the incorporation of Pgx into  
471 their curricula.

472 Incorporation of personal pharmacogenetic testing into pharmacy school  
473 curricula is a simple and efficacious method of educating our future health care  
474 professionals. Personal pharmacogenetic testing continues at UCSF through the School  
475 of Pharmacy's curricular BPS 115 course, with further goals of permanently  
476 incorporating it into this course. We believe that the new era of Precision Medicine  
477 ushered in by President Obama's Precision Medicine Initiative will only be successful if  
478 coupled with education of a new generation of health care providers. Herein, we have  
479 demonstrated that this innovative and student-led initiative has a significantly positive  
480 impact on the next generation of pharmacists, who by law will have an expanding role  
481 as the front line providers of healthcare<sup>26</sup> as we transition into an era of precision  
482 medicine.

483

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487

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Enzyme (reference)	Function	Variant Allele Frequency (decreased function) by Race
CYP2D6 <sup>27-29</sup>	Affects large numbers of drugs, notably analgesics, tamoxifen, and antidepressants and medications for attention deficit disorder.	Black: 0-5% Caucasian: 5-14% Asian: 0-1%
CYP2C19 <sup>28-30</sup>	Affects cardiovascular drugs including clopidogrel and proton pump inhibitors and some antidepressant medications	Black: 5% Caucasian: 2-5% Asian: 19%
UGT1A1 <sup>31</sup>	Affects some anticancer drugs and is responsible for hyperbilirubinemia induced by Gilbert's syndrome.	Black: 19% Caucasian: 8% Asian: 2%
HLA*5701 <sup>32</sup>	When present can cause Stevens Johnson Syndrome and delayed hypersensitivity mostly among Asians.	Black: 1% Caucasian: 6-7% Asian: up to 20%
IL28b <sup>33</sup>	C/C Alleles predicts drug efficacy towards chronic hepatitis C infections	Black: 24-50% Caucasian: 8-13% Asian: 0-1%

Characteristic	Genotyped Group N = 73	Non-Genotyped Group N = 25
Percent female*	71.2	60.0
Race/Ethnicity	N (%)	N (%)
Hispanic	0 (0.0%)	1 (4.0%)
Black	1 (1.40%)	1 (4.0%)
White	15 (20.5%)	4 (16.0%)
Asian	41 (56.2%)	17 (68.0%)
Other	14 (19.2%)	2 (8.00%)
Pacific Islander	2 (2.70%)	0 (0.00%)
*: P-value < 0.05		

Table 3: Reflections of Genotyped and Non-Genotyped Group			
<b>Genotyped Group N = 73</b>			
<b>Question</b>	<b>Disagree + Strongly Disagree, N (%)</b>	<b>Neutral, N (%)</b>	<b>Agree + Strongly Agree, N (%)</b>
Glad to have participated in Pgx testing	3.00%	8.00%	89.0%
I believe I have a better understanding of Pgx principles	1.40%	13.60%	85.0%
Felt more engaged because I had undergone Pgx testing	4.00%	19.0%	77.0%
My participation reinforced concepts taught in BPS 115	2.70%	13.8%	83.5%
<b>Non-Genotyped Group N = 25</b>			
<b>Question</b>	<b>Disagree + Strongly Disagree, N (%)</b>	<b>Neutral, N (%)</b>	<b>Agree + Strongly Agree, N (%)</b>
I regret not participating in Pgx	20%	20%	60%
Classmates Pgx results reinforced concepts	4.0%	28%	68%
I am interested in participating in more comprehensive genetic tests	4.0%	28%	68%
If offered again, I would undergo Pgx testing	8.0%	32%	60%

Figure 1: Change in Likert Score for Knowledge

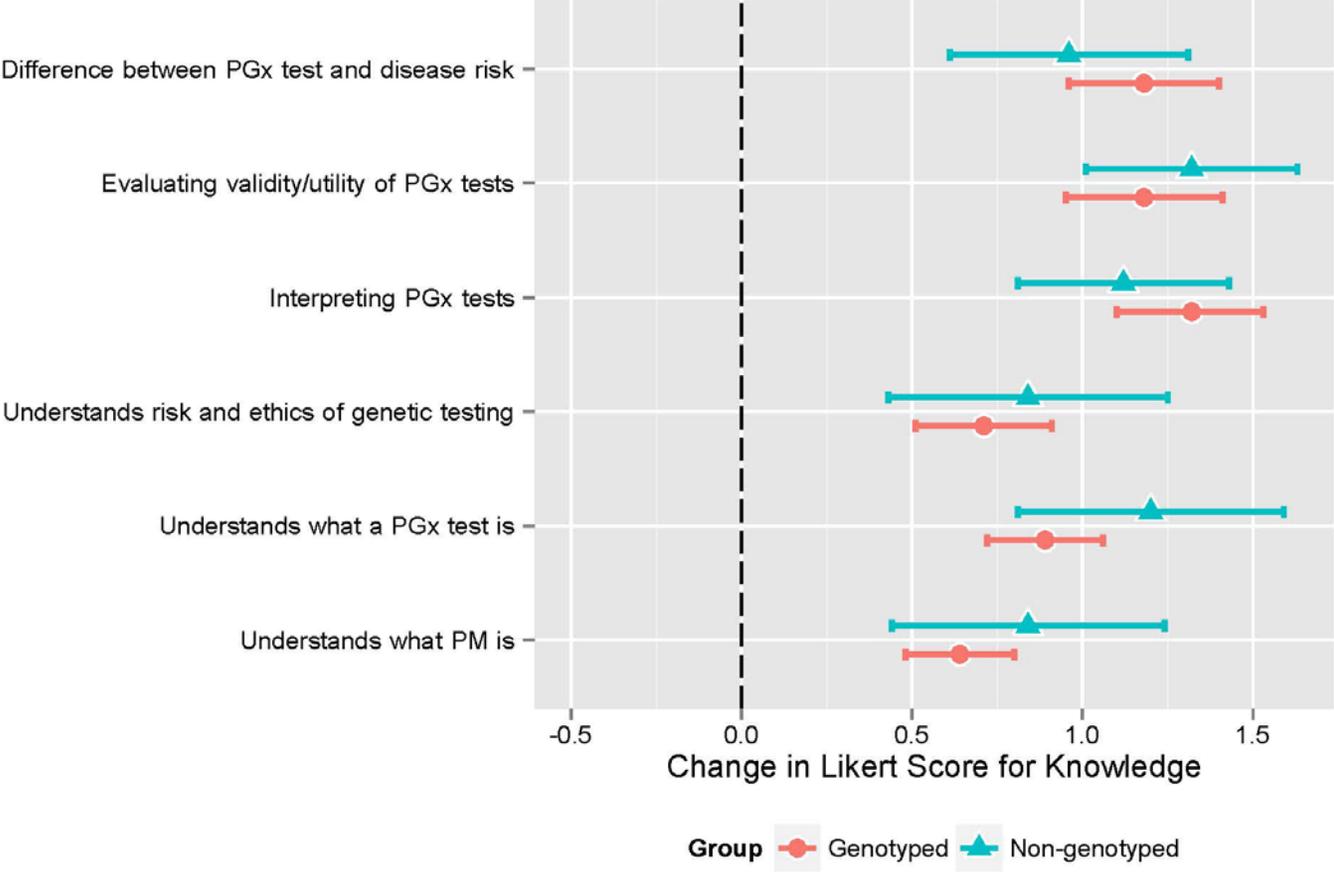
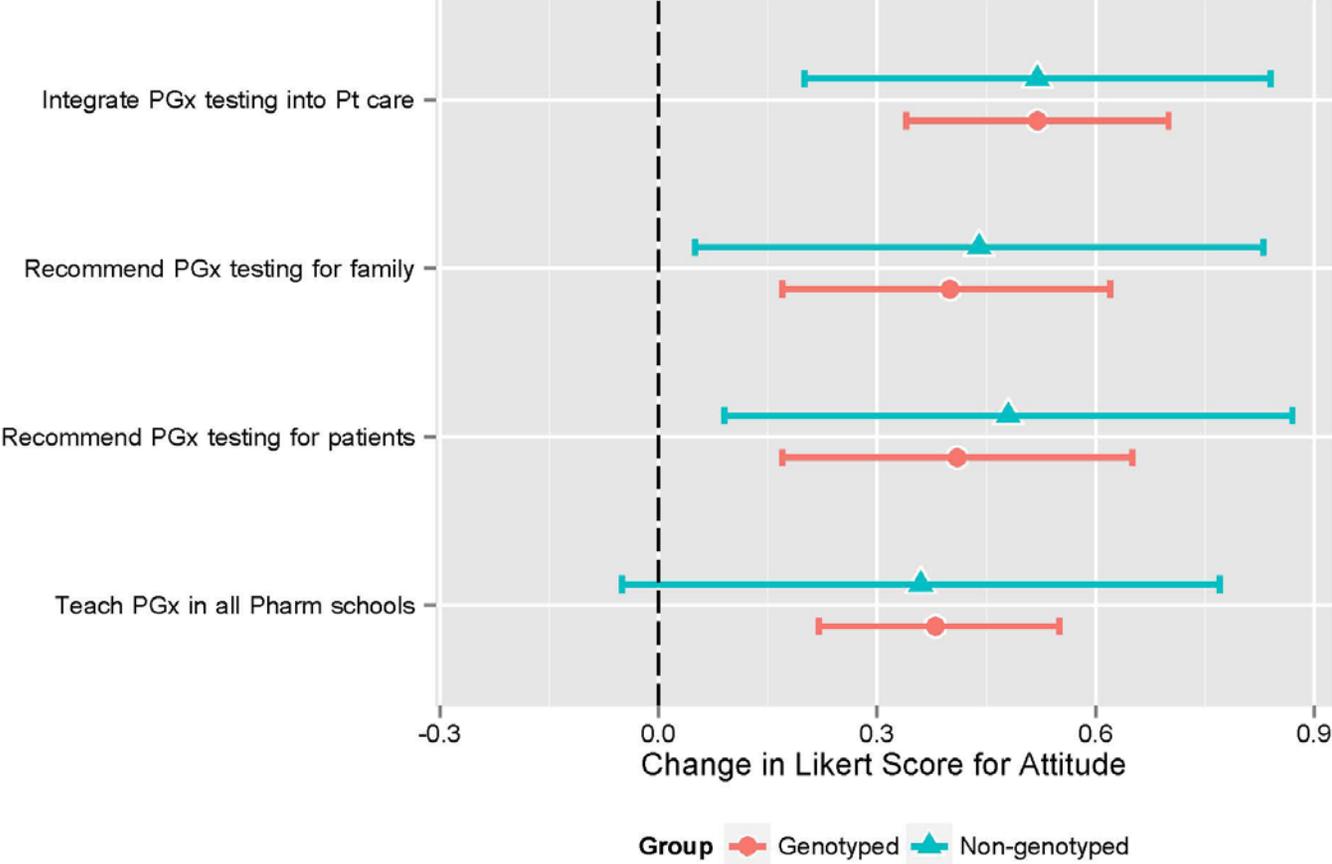


Figure 2: Change in Likert Score for Attitude



Supplementary Table 1. Knowledge and Attitude Assessment Questions from Pre and Post Survey		
	Genotyped (N=73) Effect Size; 95% CI	Non-Genotyped (N=25) Effect Size; 95% CI
<b>Knowledge</b>		
1. I understand what precision medicine is.	0.64; 0.48-0.80	0.84; 0.44-1.24
2. I understand what a pharmacogenetic test is.	0.89; 0.72-1.06	1.20; 0.81-1.59
3. I understand how a pharmacogenetic test differs from a genetic test for disease risk.	1.18; 0.96-1.40	0.96; 0.61-1.31
4. I am aware of the types of knowledge and resources needed to interpret a pharmacogenetic test result.	1.32; 1.10-1.53	1.12; 0.81-1.43
5. I understand how to evaluate the clinical validity and utility of a pharmacogenetic test.	1.18; 0.95-1.41	1.32; 1.01-1.63
6. I understand the risks, benefits, and ethical considerations of personal genetic testing.	0.71; 0.51-0.91	0.84; 0.43-1.25
<b>Attitude</b>		
1. The use of personal genetic information in health care is beneficial to patients.	0.33; 0.16-0.50	0.20; -0.16-0.56
2. The use of personal genetic information in health care may cause unnecessary harm to patients.	0.03; -0.26-0.31	0.32; -0.21-0.85
3. In addition to factors like age, race, and drug interactions, genetic information is an important consideration during routine clinical practice.	0.26; 0.04-0.48	0.28; -0.03-0.59
4. I would recommend pharmacogenetic testing for a patient.	0.41; 0.17-0.65	0.48; 0.09-0.87
5. I would recommend pharmacogenetic testing for a family member.	0.40; 0.17-0.62	0.44; 0.05-0.83
6. Pharmacogenetic testing, when applicable, should be integrated into patient care.	0.52; 0.34-0.70	0.52; 0.20-0.84

7. Pharmacists should be trained to interpret and apply pharmacogenetic test results.	0.30; 0.13-0.48	0.44; 0.16-0.72
8. Pharmacogenetics should be integrated into the curricula at all pharmacy schools.	0.38; 0.22-0.55	0.36; -0.05-0.77
9. Pharmacogenetics will likely play an important role in my future career.	0.10; -0.10-0.29	0.28; -0.07-0.63
10. Pharmacists play a crucial role in the future of precision medicine.	0.22; 0.06-0.38	0.24; -0.09-0.57
<b>Reflection</b>		
1. I am glad that I participated in the pharmacogenetic testing.		
2. I believe that I have a better understanding of the principles of pharmacogenetics on the basis of having undergone personal pharmacogenetic testing		
3. I felt more personally engaged during BPS115 because I had undergone the pharmacogenetic testing.		
4. My participation in the pharmacogenetic testing reinforced the concepts taught in BPS115		
5. I regret that I did not participate in the pharmacogenetic testing.		
6. Seeing my classmates' genetic results reinforced the concepts taught in BPS115		
7. I would be interested in participating in more comprehensive genetic testing to learn about other traits.		
8. If offered to me again, I would choose to undergo pharmacogenetic testing.		